

# A Prospective Observational Study on Clinical Endpoints in Patients with Brain Metastases Undergoing Whole Brain Radiation Therapy (WBRT)

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## Abstract

**Aim:** The aim of the study is to assess the measures of quality of life (QoL), symptoms, and overall performance status of brain metastases patients and record the acute side effects of whole brain radiation therapy.

**Methods:** A prospective observational study was performed on brain metastases patients who are diagnosed using a brain CT scan or MRI receiving WBRT. The quality of life and symptoms are assessed by using QLQ C-30 and BN-20 questionnaires, and performance status is assessed by using ECOG and recorded acute side effects during the whole brain radiation therapy.

**Results:** The patient's quality of life and symptoms are collected through the EORTC QLQ C-30 and QLQ BN-20 questionnaires. Wilcoxon signed-ranks test was used to examine the differences in baseline and follow-up measures, at the level of significance (alpha) p-value < 0.05 considered statistically significant. In C-30 majority of scales have not resulted in significant improvement at the 1-month of follow-up except for nausea and vomiting and constipation. In BN-20 only headache, seizures, and drowsiness resulted in significant improvement at the 1-month follow-up.

**Conclusion:** Overall, there is no significant improvement in patients in the majority of QLQc30- and BN-20 scale items and the performance status of patients after whole brain radiation therapy. Along with these other factors like extracranial disease burden also can have an effect on the patient's condition. So, there is a need for further advancements in the treatment of patients with brain metastases for the betterment of care in the future.

**Keywords:** Brain metastases • Whole brain radiation therapy (WBRT) • Quality of life • Performance status

## Introduction

Brain metastases are one of the common complications of cancer, with 20% to 40% of all cancer patients developing secondary brain malignancies, this has a significant impact on morbidity and mortality [1]. Their best course of treatment is still up for debate, particularly in terms of the medical care delivered [2]. Patients suffering from brain metastases experience severe symptoms like headache, seizures, nausea and vomiting, motor imbalances, neurological problems, etc., but in some instances, patients are asymptomatic [3].

Generally, patients develop single metastases or multiple metastases in the brain, in the case of a single tumor, surgical resection or surgical resection with WBRT or SRS may be used to optimize the patient's condition. But in the case of multiple metastases, the tumors will be large or maybe micrometastases, so in this condition, surgery is not the first choice of therapy.

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The whole-brain radiation therapy will be delivered to control the tumor progression and its effects.

The WBRT is considered a standard treatment for brain metastases patients, the primary goal of treatment is to alleviate symptoms, and enhance overall survival while preserving an acceptable quality of life. Typically, radiation delivered to the brain is 3000 cGy (30 Gy) in 10 fractions (standard dose) or 2000 cGy (20 Gy) in 5 fractions (in poor prognosis patients) [2].

So whole-brain radiation therapy (WBRT) is mostly used as palliative care in case of brain metastases patients, to palliate symptoms, improve quality of life and enhance overall survival in patients with brain metastases [2]. During the literature review, there are different opinions on the treatment benefits and controversial statements on the quality of life of brain metastases patients after the WBRT, Steinmann et.al assessed the quality of life of brain metastases patients at baseline and three months follow-ups resulted in moderate deterioration in several QoL domains after palliative wbrt, they further suggested the subjective benefit or burden from such therapy has to be addressed in future research [4]. The aim of our study is to assess the measures of quality of life (QoL), symptoms, and overall performance status of brain metastases patients and record the acute side effects of whole brain radiation therapy.

## Materials and Methods

A prospective observational study was conducted on brain metastases patients who are diagnosed using a brain CT scan or MRI receiving WBRT after institutional ethics committee (IEC) approval. The study was conducted for six months in the radiation oncology department, total 60 patients are participated. The recruitment of patients in the study was done by obeying the

study's inclusion criteria, patients with brain metastases receiving WBRT of age groups >18 years, and patients who received chemotherapy and radiation therapy/surgery for primary cancer are included in the study. The patients <18 years, pregnant and lactating women, patients with primary brain tumors, patients with hematological malignancies, and with significant cognitive impairment, previously treated with WBRT are excluded from the study.

The quality of life (QoL) and symptoms are assessed by using QLQ C-30 [5,6] and QLQ BN-20 [7] questionnaires and performance status is assessed by using ECOG (Eastern Cooperative Oncology Group) [8] performance grade at baseline and 1-month follow-up. Recorded the acute side effects of the patient experienced during WBRT.

The SPSS V22.0 is used for statistical analyses, and the descriptive statistics are applied for patient demographic details, performance status, and acute side effects. The quality of life and symptoms scores were analyzed for the normal distribution by histograms, normality Q-Q plots, and Shapiro Wilk test (If the significant value of the Shapiro-Wilk test is >0.05, the data is considered normally distributed. If it is <0.05 the data is significantly deviating from the normal distribution) for statistical analysis. The data of Quality-of-life scores (C-30) and symptoms (BN-20) are not normally distributed so Wilcoxon signed-rank test (non-parametric test) is applied for statistical analysis. Results were considered significant if the significance level of a p <0.05 (95% Confidence interval).

## Results

A total of 60 patients participated in the study fulfilling the inclusion and exclusion criteria. In which 55 patients completed follow-up of one month and 1 patient treatment is stopped due to severe fatigue during radiotherapy, 1 patient did not respond during follow-up, and 3 patients died within one month of follow-up after whole-brain radiation therapy. The range of age groups is 18-77 years with males being 20(33.33%) and females being 40(66.67%). The median age of males is 58 and females is 49, and the overall median of both males and females age is 51.50. In 60 patients, 20 (33.33%) patients have

been diagnosed with brain metastases along with primary cancer diagnosis and 40 (66.67%) patients have been diagnosed with brain metastases during follow-up of primary cancer. The average time for patients' primary cancer metastases to the brain was 15.65 months. The most common brain metastases that occur from primary cancers are lung cancer (49%), breast cancer (28%), and other cancers like git cancers (8%), renal cancer (5%), ovary and cervix cancers (3%), rectum cancer (2%), and metastasis from unknown origin (MUO) (2%). The performance status of patients with brain metastases plays the main role. The grading of performance status is done with ECOG (Eastern Cooperative Oncology Group) performance scale from 0 to 4 at baseline and follow-up results p-value (0.08 > 0.05) representing that there is no significant improvement in the performance status of the patients [shown in (Table 1)].

The patient's quality of life and symptoms are collected through the EORTC QLQ C-30[6] and QLQ BN-20 questionnaires. Wilcoxon signed-ranks test was used to examine the differences in baseline and follow-up measures, at the level of significance (alpha) p-value < 0.05 considered statistically significant. EORTC QLQ C-30 [shown in (Table 2) is a 30 items questionnaire that consists of global health status/QoL and functional scales, and symptoms scales/items. Global health status (GHS) grade ranges from 1(very poor) to 7 (excellent). The functional scale comprises five scales: physical functioning, role functioning, emotional functioning, cognitive functioning, and social functioning, for all functional scale's grades, ranging from 1(Not at all), 2(A little bit), 3(Quite a bit), 4(Very much). Symptom's scale consists of 9 items, with grades ranging from 1(Not at all) to 4(Very much) similar to functional scales.

The mean values of global health status/QoL at baseline (49.44) and one-month follow-up (51.87) with a p-value (0.56 > 0.05), statistically representing there is no significant improvement of GHS/QoL during one month of follow-up from baseline after wbrt. The mean values of functional scale items like, Physical functioning at baseline (45.02) and one-month follow-up (47.89) with a p-value(0.68 > 0.05), role functioning at baseline (35.69) and one-month follow-up (35.84) with a p-value (0.99 > 0.05), emotional functioning at baseline (68.53) and one-month follow-up (73.98) with a p-value (0.13 > 0.05), cognitive functioning at baseline (72.22) and one-month follow-up (75.18) with

**Table-1.** Performance status of patients at baseline and follow-up after wbrt.

Ecog Grades	Baseline	Percentage of baseline	Follow-up (1 month)	Percentage of follow-up	P-Value
0	1	1.83%	0	0.00%	0.08
1	5	9.09%	9	16.38%	
2	22	40%	25	45.45%	
3	20	36.36%	15	27.27%	
4	7	12.72%	6	10.09%	

**Table 2.** Mean scores of C-30 items at baseline and follow-up after wbrt.

Qlq c-30	Baseline	Follow-up (1-month)	P-values
GHS/QOL	49.44	51.87	0.56
Functional scale			
Physical functioning	45.02	47.89	0.68
Role functioning	35.69	35.84	0.99
Emotional functioning	68.53	73.98	0.13
Cognitive functioning	72.22	75.18	0.21
Social functioning	69.53	74.55	0.16
Symptoms scale			
Fatigue	55.87	52.35	0.45
Nausea & vomiting	30.45	17.40	0.02*
Pain	47.49	41.24	0.23
Dyspnoea	35.58	27.73	0.16
Insomnia	22.33	28.98	0.11
Appetite loss	27.71	34.36	0.27
Constipation	19.91	9.62	0.01
Diarrhoea	1.2	2.4	0.45

Here \* represents p-values are <0.05

a p-value (0.21 > 0.05), social functioning at baseline (69.53) and one-month follow-up (74.55) with a p-value (0.16 > 0.05), here all the functional scale items, statistically representing there is no significant improvement during one month of follow-up from baseline after whole-brain radiation therapy.

The mean values of symptoms scale items are, fatigue at baseline (55.87) and one-month follow-up (52.35) with a p-value (0.45 > 0.05), pain at baseline (47.49) and one-month follow-up (41.24) with a p-value (0.23 > 0.05), dyspnoea at baseline (35.58) and one-month follow-up (27.73) with a p-value (0.16 > 0.05), insomnia at baseline (22.33) and one month follow-up (28.98) with a p-value (0.11 > 0.05), appetite loss at baseline (27.71) and one-month follow-up (34.36) with a p-value (0.27 > 0.05), diarrhoea at baseline (1.2) and one-month follow-up (2.4) with a p-value (0.45 > 0.05), here most of the symptoms scale items, statistically representing there is no significant improvement during one month of follow-up from baseline after whole-brain radiation therapy except the nausea and vomiting at baseline (30.45) and one-month follow-up (17.40) with a p-value (0.02 < 0.05) and constipation at baseline (19.91) and one-month follow-up (9.62) with a p-value (0.01 < 0.05), statistically representing there is a significant improvement at one month of follow-up from baseline after whole-brain radiation therapy.

EORTC QLQ BN-20 (Table 3) is 20 questions brain symptoms questionnaire, it is a supplementary questionnaire module to be employed in conjugation with QLQ C-30. All these questions are characterized into 11 single items (Future uncertainty, headaches, visual disorder, seizures, motor dysfunction, communication deficit, drowsiness, hair loss, itchy skin, weakness of legs, bladder control), for all these items grades ranging from 1 (not at all), 2(a little bit), 3(quite a bit), 4(very much). the mean scores of future uncertainty at baseline (21.07) and one-month follow-up (17.73) with a p-value (0.20 > 0.05), visual disorder at baseline (9.16) and one-month follow-up (9.51) with a p-value (0.88 > 0.05), motor dysfunction at baseline (24.33)

and one-month follow-up (21.76) with a p-value (0.51 > 0.05), communication deficit at baseline (16.20) and one-month follow-up (14.09) with a p-value (0.66 > 0.05), itchy skin at baseline (5.42) and one-month follow-up (6.02) with a p-value (0.87 > 0.05), weakness at baseline (39.78) and one-month follow-up (36.73) with a p-value (0.49 > 0.05), bladder control at baseline (8.47) and one-month follow-up (12.07) with a p-value (0.37 > 0.05) here the above mentioned items, statistically representing there is no significant improvement during one month of follow-up from baseline after whole-brain radiation therapy except the headaches at baseline (62.27) and one-month follow-up (34.96) with a p-value (0.00 < 0.05), seizures at baseline (8.44) and one-month follow-up (1.8) with a p-value (0.03 < 0.05), drowsiness at baseline (43.35) and one-month follow-up (31.31) with a p-value (0.04 < 0.05), statistically representing there is a significant improvement at one month of follow-up from baseline after whole-brain radiation therapy. The mean scores of hair loss at baseline (2.40) and one-month follow-up (39.29) showed there is a significant difference between baseline and follow-up with a p-value (0.00 < 0.05), statistically representing there is a significant worsening of hair loss at one month of follow-up from baseline after whole brain radiation therapy.

The acute side effects of whole-brain radiation therapy are recorded during the treatment shown in (Table 4). A total of 182 side effects are recorded during the treatment, the most common side effects encountered during the wbrt is fatigue (26.92%), hair loss (20.33%), headache (12.09%), vomiting (7.69%), nausea (6.59%), skin and scalp changes (6.69%), somnolence (7.14%), dysarthria (slurred speech) (3.85%), dysphasia (0.55%), fever (3.30%), memory loss (2.20%), seizures (1.65%), drowsiness (0.55%), epiphora (0.55%).

## Discussion

Metastatic brain cancers may be treated using WBRT, which has been

**Table 3.** Mean scores of BN-20 items at baseline and follow-up after wbrt.

Qlq bn-20	Baseline	Follow-up (1-month)	P-values
Future uncertainty	21.07	17.73	0.20
Headaches	62.27	34.96	0.00*
Visual disorder	9.16	9.51	0.88
Seizures	8.44	1.8	0.03*
Motor dysfunction	24.33	21.76	0.51
Communication deficit	16.20	14.09	0.66
Drowsiness	43.35	31.31	0.04*
Hairloss	2.40	39.29	0.00*
Itchy skin	5.42	6.02	0.87
Weakness of leg	39.78	36.73	0.49
Bladder control	8.47	12.07	0.37

Here \* represents p-values are <0.05

**Table 4.** Acute side effects.

Side effects	Frequency	Percentage
Fatigue	49	26.92%
Hairloss	37	20.33%
Headache	22	12.09%
Vomitings	14	7.69%
Nausea	12	6.59%
Skin and scalp changes	12	6.69%
Somnolence	13	7.14%
Dysarthria	7	3.85%
Dysphasia	1	0.55%
Fever	6	3.30%
Memory loss	4	2.20%
Seizures	3	1.65%
Drowsiness	1	0.55%
Epiphora (excessive tearing)	1	0.55%
<b>Total</b>	<b>182</b>	<b>100%</b>

available for a long time, especially when there are multiple tumors. Fractions are typically administered in a sequence of five to fifteen doses. WBRT typically uses dosage of 30 Gy administered in 10 daily fractions. It has been authorized as palliative therapy for brain metastases because of its ability to control neurologic symptoms and reduce disease burden in several clinical investigations [9]. Our primary objective of the study is to assess the quality of life and symptoms control in brain metastases patients, all patients received 30 Gy in 10 fractions. The main findings from our study are the items of QLQ C-30 like nausea and vomiting, constipation resulted in significant improvement from baseline during the 1-month follow-up, but all other GHS, functional scales items, and remaining symptoms scale items resulted in no significant improvement. from QLQ BN-20 questionnaires, headaches, seizures, and drowsiness, result in significant improvement after whole-brain radiotherapy at 1-month of follow-up. Studies by Gerrard et al. and Roos et al., which are similar to the current one, also used the QLQ-C30 and the QLQ-BN20 to evaluate QOL in patients receiving radiation for brain metastases [10,11].

The brain metastases patients used to have a one-month survival rate, but steroids extended it to two months. WBRT is usually utilized as an adjuvant treatment following surgical resection or in the case of multiple metastases that aren't surgically resectable, then this is used as palliative care (for symptoms improvement) [2]. The use of whole-brain treatment increased the median survival duration to 4–6 months, according to reports but our study primarily concentrated on the quality of life, symptoms, and performance status of patients. The performance status of the patient resulted in no significant improvement after wbrt during follow-up. The Radiation Treatment Oncology Group (RTOG) conducted a series of clinical studies in the 1970s to investigate the effectiveness of radiation therapy and to determine the best fractionation schemes, 30 Gy in 10 fractions is the standard dose in the majority of patients receiving WBRT [12]. The patients with poor performance status or uncontrolled extracranial disease burden, 20 Gy in 5 fractions can be considered [12]. Complications of whole brain radiation therapy can be acute or delayed, in our study only acute side effects had been recorded the most common ones are fatigue, hair loss, headache, vomiting and nausea, skin and scalp changes, etc. Many studies have recently been undertaken to evaluate various radiation approaches as independent treatment modalities to their combinations [9]. Other research focuses on combining radiation with neurosurgery, for example (surgery + wbrt, srs + wbrt, etc.) this combination of methods resulted in good improvements instead of only wbrt, also with fewer side effects [9,12].

## Limitations

The study limitations were that the study was conducted in a single cancer institution, and the sample size of the study was small due to study duration was only six months.

## Conclusion

From above study, we concluded that only nausea & vomiting, and constipation, from the QLQ C-30 questionnaires, headaches, seizures, and drowsiness, from the QLQ BN-20 questionnaires, result in significant improvement after whole-brain radiotherapy at one month of follow-up. Overall, there is no significant improvement of patients in the majority of QLQc30- and BN-20 scale items and the performance status of patients after whole brain

radiation therapy. Along with these other factors like extracranial disease burden also can have an effect on the patient's condition. So, there is a need for further advancements in the treatment of patients with brain metastases for the betterment of care in the future.

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## Conflict of Interest

We have no conflicts of interest to disclose.

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